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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/723,144	11/25/2003	Robert J. Ternansky	474930-4 34433/US/3/AMP/S	9257

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EXAMINER	
CORDERO GARCIA, MARCELA M	
ART UNIT	**PAPER NUMBER**
1654	
MAIL DATE	**DELIVERY MODE**
10/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/723,144	TERNANSKY ET AL.	
	Examiner	Art Unit	
	Marcela M. Cordero Garcia	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5,19,20,22-40,42,43,55,58,59 and 66-71* is/are pending in the application.

4a) Of the above claim(s) *23-24, 26-29,32-43,66-69 and 71* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 5, 19-20, 22, 25, 30-31, 58-59 and 70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *05/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

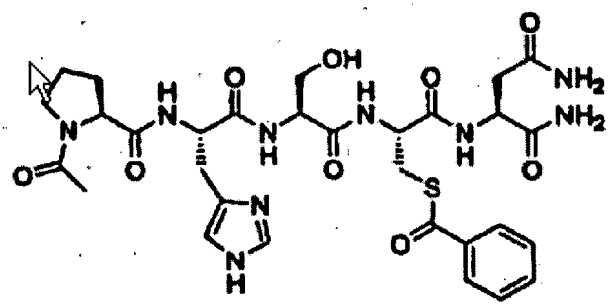
This Office Action is in response to the reply received on May 15, 2007.

Claims 1, 5, 19-20, 22-40, 42-43, 55, 58-59, 66-71 are pending in the application. Claims 1, 26, 35, 38, 40, 59 have been amended. Claims 66-71 have been added.

Any rejection from the previous office action, which is not restated here, is withdrawn.

Claims 1, 5, 19-20, 22-40, 42-43, 55, 58-59, 66-71 are presented for examination on the merits.

Applicants elected the species of Formula I wherein R^1 is acyl (i.e., $-C(O)CH_3$, x is 1, A is Pro, y is 1, B is His, z is 1, C is Ser, a is 1, R^2 is $-(CH_2)_mS(O)_nR^5$, m is 1, n is 0, R^5 is acyl (i.e., C(O)Ph), b is 1, R^3 is $-CH_2CONH_2$, R^4 is $-NR^6R^7$ and R^6 and R^7 are hydrogen, as indicated in the following structure:



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in the reply filed on May 31, 2005 is acknowledged, with claims 1, 5, 19-20, 22, 25, 30-31, 58-59 and new claim 70 are readable thereon. This species was previously found to be free of the prior art, however, upon reconsideration, the species is now rejected

under 103(a). Claims 23-24, 26-29, 32-43, 66-69 and 71 are withdrawn as not drawn to the examined group/species.

Withdrawn Rejections

The previous new matter rejection of claims 1, 5, 19-20, 22-26, 30-31, 34-39, 55-56, 58-59 has been withdrawn because, in light of the changes made during prosecution to the definitions of a, b, x, y, z, and R_1 in the main body of the claim, any limitations which might have been imposed by the provisos are now effectively imposed by the main body of the claim.

The previous 103(a) rejection of claims 1, 5, 19-20, 22-24, 26, 35-39, 55-56 and 58-59 as being unpatentable over Livant (US 6,001,965, citation A19 in the IDS of 08/11/06) is withdrawn in view Applicants' amendments eliminating R_5 = methyl.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 5, 19-20, 22, 25, 30-31, 58-59 and new claim 70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Livant (US 6,001,965, citation A19 in the IDS of 08/11/06) in view of Livant (WO 02/057786, citation B1 in the IDS of 5/15/07) and in view of Greene et al. (Protective Groups in Organic Synthesis, 1999).

Livant '965 teaches a high activity anti-angiogenic compound Ac-Pro-His-Ser-Cys-Asn-NH_2 (e.g., column 26, 27-40, Figures and Examples 9-13), and synthesis of peptide analogs thereof. Livant teaches that during synthesis of the peptides it can be necessary to protect potentially reactive groups other than the amino and carboxyl groups intended to react (e.g., column 12, lines 60-67). Livant '786 teaches synthetic protecting groups are those groups which prevent undesirable reactions involving unprotected functional groups, and encompass, e.g., acyl, benzyl and benzoyl (e.g., bridging paragraph between pages 13-14).

Livant does not expressly teach protecting the cysteine in Ac-Pro-His-Ser-Cys-Asn-NH_2 with, e.g., acyl, acetyl, benzoyl or benzyl as in Ac-Pro-His-Ser-Cys(protecting agent)-Asn-NH_2.

Greene et al. teach protecting reactive thiol groups such as in cysteine [i.e., Cys(protecting agent)] during peptide and protein synthesis using protecting agents which encompass, e.g., acyl (e.g., pages 482-484), acetyl (e.g., page 482), benzoyl (e.g., pages 482-483) and benzyl (page 458-463).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the composition Ac-Pro-His-Ser-Cys-Asn-NH_2 of Livant '786 and '965 by protecting the cysteine with, e.g., benzoyl. The skilled artisan would have been motivated to do so because Livant '965 teaches protecting groups would prevent undesirable reactions (e.g., column 12, lines 60-67) and Livant '786 teaches protecting groups are those groups which prevent undesirable reactions involving unprotected functional groups, and encompass, e.g., benzoyl. There would have been a reasonable expectation of success, given that Greene et al. teach protecting agents for reactive thiol groups useful in peptide and protein synthesis, and specifically the amino acid cysteine [i.e., Cys(benzoyl) (e.g., pages 482-483).

The adjustment of particular conventional working conditions (e.g., selecting specific D/L stereochemistry, e.g., column 3, lines 39-40 as in claims 19-20) is deemed merely a matter of judicious selection and routine optimization that is well within the purview of the skilled artisan. As such, it would have been obvious to one skilled in the art at the time of invention to determine all optimum and operable conditions (e.g., selecting specific D/L stereochemistry, e.g., column 3, lines 39-40 as in claims 19-20), because such conditions are art-recognized result-effective variables that are routinely determined and optimized in the art through routine experimentation ("[W]here the

general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.". *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). See MPEP 2145.05). One would have been motivated to determine all optimum and operable conditions in order to achieve the highest yield of the highest purity product in the most efficient manner. One would have had a reasonable expectation for success because such modifications are routinely determined and optimized in the art through routine experimentation.

From the teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to

be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 5, 19-20, 22, 25, 30-31, 58-59 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 64-65 of copending Application No. 10/722,843. Claims 64-65 of '843 encompasses therapeutic agents attached to the fourth amino acid, which is not excluded by the instant claims, as, e.g., the cysteine can be substituted by ethyl propyl, butyl, alkenyl, alkyinyl, substituted alkyl, acyl, substituted acyl, aryl, substituted aryl, arylalkyl, substituted arylkalkyl, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroalkyl, oxycarbonyl or substituted oxycarbonyl. Please note that many therapeutic agents, e.g., doxorubicin of claim 75 of '843 can be attached to the substituted cysteine, such as doxorubicin, a known cytotoxic agent which reads upon R_5 equals to "substituted aryl" as encompassed by the instant claims. Further, the instantly claimed broad formula (I) of the instant application encompasses and/or is encompassed by the claimed broad formula (V) of Application '843.

This is a provisional obviousness-type double patenting rejection.

Conclusion

No claim is allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marcela M. Cordero Garcia whose telephone number is (571) 272-2939. The examiner can normally be reached on M-Th 7:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia J. Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Art Unit 1654

MMCG 09/07

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